A library in the group updated the review by searching 6 electronic databases from September 2011 until January 2015. They included randomized and non-randomized studies that examined cognitive enhancers (donepezil, rivastigmine, galantamine, and memantine) alone or in combination compared to each other or placebo. The outcomes of interest were: cognition, function, behaviour, global status, mortality, and harms (nausea, vomiting, diarrhea, bradycardia, headache, falls, and all serious adverse events (SAEs)). Screening of literature search results, data abstraction, and risk of bias appraisal were completed independently by two reviewers. Random-effects Bayesian NMA was conducted for outcomes with a connected network of treatments.

**What did the study find?**
- 186 studies including 106 RCTs, 20 non-randomized clinical-trials, 8 cohort studies, and 53 companion reports were included.
- Donepezil and rivastigmine improved cognition compared to placebo, but only donepezil showed a clinically important difference on the ADAS-cog scale. All cognitive enhancers improved cognition compared to placebo in patients with mild-to-moderate AD and donepezil improved cognition compared to placebo in patients with severe AD.
- All cognitive enhancers improved global status compared to placebo and galantamine demonstrated a clinically meaningful effect compared to placebo, donepezil, rivastigmine, and donepezil+memantine; no differences were observed between the agents for function or behaviour.
- Donepezil, rivastigmine, and galantamine all caused more gastrointestinal side effects compared to placebo; no differences between agents were observed for SAEs, bradycardia or falls.
- Rivastigmine decreased the risk of mortality compared to placebo and memantine but caused more headaches compared to placebo.
- Rivastigmine patch demonstrated similar efficacy in improving cognition but caused significantly less nausea than oral rivastigmine.

**Implications**
As this is a rapidly updated review, results should be interpreted with caution. However, these findings demonstrate the need for patient decision aids to help individuals with AD and their families to choose the right medication for their treatment goals. Future research in this area will focus on analysing individual patient data in a network meta-analysis.

**Authors:** Andrea C. Tricco, Huda M. Ashoor, Patricia Rios, Jemila Hamid, John D. Ivory, Paul A. Khan, Fatemeh Yazdi, Charlene Soobiab, Marco Ghassemi, Erik Blondal, Joanne Ho, Sharon E. Straus

For more information, please contact Dr. Andrea Tricco: TriccoA@smh.ca

**Funded by:**